

Congenital sacrococcygeal PNET and chemotherapy

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ABSTRACT

We present the case of a congenital localised sacrococcygeal primitive neuroectodermal tumor treated aggressively with surgical resection and modified age-appropriate adjuvant chemotherapy. The conventional combination chemotherapy of vincristine, adriamycin, cyclophosphamide, ifosfamide and etoposide was modified to a regimen including vincristine, adriamycin, cyclophosphamide and actinomycin in order to minimise the predicted toxicity in this age group. Adjuvant "induction" chemotherapy commenced at 4 weeks of age and consisted of four cycles of vincristine, adriamycin and cyclophosphamide at 50%, 75%, 75% and 100% of recommended doses (vincristine 0.05 mg/kg, adriamycin 0.83 mg/kg daily × 2, cyclophosphamide 40 mg/kg) at 3-weekly intervals. This was followed by four cycles of "maintenance" chemotherapy with vincristine (0.025 mg/kg), actinomycin (0.025 mg/kg) and cyclophosphamide (36 mg/kg) at full recommended doses. Cardioxane at a dose of 16.6 mg/kg was infused immediately prior to the adriamycin. Our patient is thriving at 19 months out from end of treatment.

Key words: *Chemotherapy, neonatal, peripheral primitive neuroectodermal tumor, primitive neuroectodermal tumor*

INTRODUCTION

Neonatal tumors represent 2% of childhood malignancies, of which teratoma and neuroblastoma are the most common types.^[1] Malignant lesions presenting in the sacrococcygeal region are most often sacrococcygeal teratomas.^[2] We present a case of a congenital localised sacrococcygeal primitive neuroectodermal tumor (PNET), of which there has only been one reported case.^[3] Our case, treated aggressively with surgical resection and modified age-appropriate adjuvant chemotherapy has had a favourable outcome to date.

CASE REPORT

A baby girl born at 42 weeks gestation via spontaneous vaginal delivery following an uncomplicated pregnancy was noted at delivery to have a fullness in her left gluteal region.

Ultrasound on Day 1 of life showed a complex solid and cystic 2.5 cm × 2.5 cm mass to the left side of the natal cleft

arising from the distal end of the coccyx. The rectum was seen directly anterior to this mass. Small foci of calcification were seen within the cystic component. Alfa-fetoprotein and βHCG were both normal.

The mass was thought to be a sacrococcygeal teratoma and was resected via an elliptical incision over the lower coccygeal region. A complete macroscopic resection was achieved. Histology showed a small round blue cell tumor with diffuse, crisp membranous CD99 immunoreactivity. Fluorescence *in situ* hybridization (FISH) was performed with an EWSR1 break apart probe (Vysis, Abbott, Illinois, U.S.A.) on tumor touch preps and demonstrated the presence of a population of nuclei with a rearrangement of this locus, which would lend support to the diagnosis of a peripheral PNET/Ewing sarcoma family tumor (PNET/ESFT). Lateral resection margins were microscopically positive for tumor cells, while deep margins were clear.

A wider resection was then performed. This included a 1-cm margin on each side of the initial resection, and extended down to the sacral fascia and posterior wall of the rectum. A small residual cartilaginous portion of coccyx was also excised. Histology of the additionally resected tissue did not show any evidence of malignant cells. Post-operative computerised tomography of the thorax as well as magnetic resonance imaging (MRI) of the brain, spine and abdomen showed no metastases or evidence of residual disease. Bone marrow aspirate revealed no evidence of tumor infiltration.

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Adjuvant “induction” chemotherapy was commenced at 4 weeks of age, consisting of four cycles of vincristine, adriamycin and cyclophosphamide (VadriaC) at 3-weekly intervals. Doses for the first cycle were at 50%, cycles 2 and 3 were at 75% and cycle 4 was at 100% recommended doses (vincristine 0.05 mg/kg, adriamycin 0.83 mg/kg daily × 2, cyclophosphamide 40 mg/kg). Cardioxane at a dose of 16.6 mg/kg was infused immediately prior to the adriamycin. Thereafter, she received four cycles of “maintenance” chemotherapy with vincristine, actinomycin and cyclophosphamide (VAC) at full recommended doses (vincristine 0.025 mg/kg, actinomycin 0.025 mg/kg, cyclophosphamide 36 mg/kg). She tolerated chemotherapy very well with no significant complications. Cardiac echocardiography remained normal throughout treatment, as did routine liver/renal-related biochemistry.

End-of-treatment MRI pelvis revealed post-operative changes only, with no residual tumor. There was no evidence of disease on her most recent follow-up MRI scan and chest X-ray at 16 months following completion of treatment. Clinically, she is thriving.

DISCUSSION

Congenital masses in the sacrococcygeal area are rare, and the differential diagnosis includes both benign and malignant lesions. Benign lesions include lipoma, hemangioma, meningocele, lymphangioma, pilonidal sinus, dermoid, myxopapillary ependymoma and epidermoid cysts.^[4] Three-quarters of sacrococcygeal teratomas are evident at birth,^[5] and these represent the majority of malignant lesions in this area.^[6] Isolated cases of other malignant lesions in the sacrococcygeal region in this age group have been published, including teratoid Wilms’ tumor,^[7] malignant Triton tumor,^[8] ependymblastoma^[9,10] and neuroblastoma.^[11] In the only congenital sacrococcygeal PNET case reported to date, primary excision was incomplete^[2] and the patient received dactinomycin and vincristine. This patient developed fatal cerebral metastases.

Congenital peripheral PNET/ESFTs are rare, and generally have a poor prognosis. Combining available data from Meazza *et al.*,^[12] and Kim *et al.*,^[13] in the 24 cases of congenital pPNET/ESFTs reported to date, less than 29% of the patients remain alive, with the majority of patients dying within 6 months of diagnosis. With a background of such a poor prognosis, aggressive curative-intent treatment with complete surgical resection together with adjuvant chemotherapy is indicated.

Chemotherapy is challenging in the neonatal period relative to potential age-related limited drug metabolism, thereby theoretically exposing the developing neonate

to excessive chemotherapy-related toxicity. For this reason, we individualized the well-recognised ESFTs VadriaC + Ifosfamide/Etoposide chemotherapy regimen to negate the predicted toxicity in this age group. VadriaC was initiated at 50% dose reduction and titrated up to full dosage if tolerated. Anthracycline-related cardiotoxicity was addressed by limiting the cumulative adriamycin dose to 150 mg/m² and by administering cardioxane prior to each adriamycin infusion. Ifosfamide was omitted because of the risk of significant nephrotoxicity, with the Ifosfamide/Etoposide component being replaced by VAC. Dosages were used as per the age-appropriate historical Children’s Oncology Group Rhabdomyosarcoma protocol D9803.^[14]

Acknowledging the limited follow-up of our patient (19 months post-completion of treatment), we consider the above-described individualized chemotherapy regimen to be effective to-date with no clinically overt treatment-related significant sequelae. We recommend considering utilising this modified VadriaC + VAC adjuvant chemotherapy regimen in the treatment of congenital ESFTs.

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